Case 1. A patient (SP), a student athlete needs to be started on gentamicin for a serious infection in the right knee. The patient is a 22 Y.O. white female, 5'7" and weighing 77 Kg. Her serum creatinine is 1.5 mg/dL and she demonstrates clear physical signs of de-hydration. The medical resident wants to know what dose of gentamicin you would recommend for traditional dosing:

Estimate IBW:

$$IBW = 45.5Kg + 2.3*(Htin.-60) \qquad = 61.6\ Kg \qquad \text{Eq. 1}$$

Estimate CrCl:

BMI = 26.6 so CrClWt = 67.8 Kg $\quad CrCl = \dfrac{(140 - Age)\cdot CrClWt}{SrCr \cdot 72} = 62.9$ ml/min Eq. 2

Population PK data for gentamicin estimates the elimination rate constant and half-life:

$$k_e = 0.015 + (0.00285 \cdot CrCl) \qquad = 0.194\ Hr.^{-1} \qquad \text{Eq. 3}$$

$$t_{1/2} = \frac{\ln 2}{k_e} \qquad = 3.6\ Hr \qquad \text{Eq. 4}$$

Estimate the volume of distribution:

$$V_{ss} = V_d\ factor \cdot DWT \qquad \text{Eq. 5}$$

$$AdjWT = IBW + 0.4(WT - IBW) \text{ (If WT > 1.3×IBW) Not so DWT} = 77Kg \qquad \text{Eq. 6}$$

$$V_{ss} = 0.15\ L/Kg \cdot 77\ Kg = 11.55\ L$$

Estimate Tau (the 5th equation in the Sawchuk-Zaske list):

$$\tau = \frac{\ln(C_{\max/\text{desired}}/C_{\min/\text{desired}})}{k_e} + t_{\text{inf}} \qquad = \frac{\ln(7/1)}{0.194\ Hr^{-1}} + 0.5\ Hr = 10.5\ Hr \qquad \text{Eq. 7}$$

Select a practical Tau (e.g. Q6H, Q8H, Q12H or Q24H) based on this estimate. Here Q12H.

Using the practical interval, estimate the new dose (the 6th eq. in the Sawchuk-Zaske list):

$$R_0 = C_{\max,\text{desired}} \cdot V_{ss} \cdot k_e \left[\frac{1 - e^{-k_e \tau}}{1 - e^{-k_e t_{\text{inf}}}}\right] \qquad \text{Eq. 8}$$

$$= 7\ mg/L \cdot 11.55\ L \cdot 0.194\ Hr^{-1} \left[\frac{1 - e^{-0.194 Hr^{-1} 12 Hr}}{1 - e^{-0.194 Hr^{-1} 0.5 Hr}}\right] = 153.1\ mg/Hr$$

$$Dose = R_0 \cdot t_{\text{inf}} \qquad = 153.1\ mg/Hr \cdot 0.5\ Hr = 76.6\ mg \qquad \text{Eq. 9}$$

Make a practical recommendation (Gentamicin is usually dosed in 10 mg increments):

80 mg Gentamicin Q12H for a Pk/Tr = 7.3/0.8 mg/L

Verify that this will give you desirable steady state peak and trough concentrations:

$$C_{ss,pk} = \frac{R_0}{V_{ss} \cdot k_e} \bullet \frac{\left(1 - e^{-k_e t_{\text{inf}}}\right)}{\left(1 - e^{-k_e \tau}\right)} \qquad \text{Eq. 10}$$

$$C_{ss,pk} = \frac{80\ mg / 0.5\ Hr.}{11.55\ L \cdot 0.194\ Hr^{-1}} \bullet \frac{\left(1 - e^{-0.194 \cdot 0.5}\right)}{\left(1 - e^{-0.194 \cdot 12}\right)} = 7.3\ mg/L$$

$$C_{ss,tr} = C_{ss,pk} \cdot e^{-k_e(\tau - t_{\text{inf}})} \qquad = 7.3\ mg/L \cdot e^{-0.194(12-0.5)} = 0.8\ mg/L \qquad \text{Eq. 11}$$

Case 2. PT is a 57 YO 5'11' male with a *Pseudomonas* pneumonia. His weight is 90 Kg and his serum creatinine is 1.2 mg/dl. Blood pressure, heart rate, skin turgor and vascular filling of neck veins indicate that SW is normally hydrated. What dose (mg) of gentamicin would you recommend for initiation of traditional dosing and what interval would you recommend?

Determine IBW: 75.3 Kg

$$IBW = 50Kg + 2.3*(Htin.-60) \qquad = 50 + 2.3*(71-60) = 75.3\ Kg \qquad \text{Eq. 1}$$

DWT: 90 Kg (Because it is not 30% over ideal)

$$AdjWT = IBW + 0.4(WT - IBW) \quad \text{(If WT > 1.3×IBW)} \qquad = 90\ Kg \qquad \text{Eq. 2}$$

Estimate CrCl.

BMI = 27.7 so CrClWt = 81.2 $CrCl = \dfrac{(140 - Age)\cdot CrClWt}{SrCr \cdot 72} = 78.0$ ml/min Eq. 3

Population PK data for gentamicin estimates the elimination rate constant and half-life:

$$k_e = 0.015 + (0.00285 \cdot CrCl) \qquad = 0.237\ Hr.^{-1} \qquad \text{Eq. 4}$$

$$t_{1/2} = \frac{\ln 2}{k_e} \qquad = 2.9\ Hr \qquad \text{Eq. 5}$$

Estimate the volume of distribution (you must know the hydration status):

$$V_{ss} = V_d\ factor \cdot DWT \qquad V_{ss} = 0.225\ L/Kg \cdot 90\ Kg = 20.25\ L \qquad \text{Eq. 6}$$

Estimate Tau (the 5th equation in the Sawchuk-Zaske list):

$$\tau = \frac{\ln(C_{\max/desired}/C_{\min/desired})}{k_e} + t_{\inf} \qquad = \frac{\ln(7/1)}{0.237\ Hr^{-1}} + 0.5\ Hr = 8.7\ Hr \qquad \text{Eq. 7}$$

Select a practical Tau (e.g. Q6H, Q8H, Q12H or Q24H) based on this estimate. Here Q8H.

You could choose tau based on half-life (just under 3) – that would be a Tau of 8 hours.

Using the practical interval, and we'll go with 8, estimate the new dose (the 6th equation in the Sawchuk-Zaske list):

$$R_0 = C_{\max,desired} \cdot V_{ss} \cdot k_e \left[\frac{1 - e^{-k_e \tau}}{1 - e^{-k_e t_{\inf}}}\right] \qquad \text{Eq. 8}$$

$$= 7\ mg/L \cdot 20.25\ L \cdot 0.237\ Hr^{-1}\left[\frac{1 - e^{-0.237\ Hr^{-1} 8Hr}}{1 - e^{-0.2371 Hr^{-1} 0.5Hr}}\right] = 255.5\ mg/Hr$$

$$Dose = R_0 \cdot t_{\inf} \qquad = 255.5\ mg/Hr \cdot 0.5\ Hr = 127.7\ mg \qquad \text{Eq. 9}$$

Make a practical recommendation (Gentamicin is usually dosed in 10 mg increments):

130 mg Gentamicin Q8H for a Pk/Tr = 7.1/1.2 mg/L

Verify that this will give you desirable steady state peak and trough concentrations:

$$C_{ss,pk} = \frac{R_0}{V_{ss} \cdot k_e} \bullet \frac{\left(1 - e^{-k_e t_{\inf}}\right)}{\left(1 - e^{-k_e \tau}\right)} \qquad \text{Eq. 10}$$

$$C_{ss,pk} = \frac{120\,mg \,/\, 0.5\,Hr.}{20.25\,L \cdot 0.237\,Hr^{-1}} \bullet \frac{\left(1 - e^{-0.237 \cdot 0.5}\right)}{\left(1 - e^{-0.237 \bullet 8}\right)} = 7.1\,mg/L$$

$$C_{ss,tr} = C_{ss,pk} \cdot e^{-k_e(\tau - t_{\inf})} = 7.1\,mg/L \cdot e^{-0.237(8-0.5)} = 1.2\,mg/L \qquad \text{Eq. 11}$$

Case 3. If we went with the 120 mg Q8H and the levels came back at 9.7 mg/L at 9:15 am and 1.6 mg/L at 07:50 am and the dose was scheduled to be given at 8:00 am, what recommendation would you make? (Since the gentamicin was started, the patient has begun to show signs of dehydration.)

Calculate the elimination rate constant:

$$k_e = \frac{\ln\left(C_{pk} / C_{tr}\right)}{t_{tr} - t_{pk}} = \frac{\ln\left(9.7/1.6\right)}{8 - 1.25} = \frac{\ln\left(9.7/1.6\right)}{6.75\,Hr.} = 0.267\,Hr^{-1} \qquad \text{Eq. 1}$$

(In terms of the dosing interval the infusion was started at t = 0, it stopped at 0.5 hr, and the pk was measured at 1.25 hr and the trough (extrapolated) was at 8 hours, therefore t_2 -t_1 is 8 - 1.25 = 6.75. Or (Tau – t_{inf} – t_{pi}) = 8 – 0.5 – 0.75 = 6.75 hours.

$$t_{1/2} = \frac{\ln 2}{k_e} = 2.6\,Hr$$

Calculate the maximum concentration:

$$C_0 = \frac{C_{pk}}{e^{-k_e\left(t_{pk} - t_{\inf}\right)}} = \frac{9.7 mg/L}{e^{-0.267 Hr^{-1}(1.25\,Hr - 0.5\,Hr)}} = 11.9\,mg/L \qquad \text{Eq. 2}$$

Calculate the volume of distribution:

$$V_{ss} = \frac{R_0}{k_e} \cdot \frac{1 - e^{-k_e t_{\inf}}}{\left(C_0 - C_{tr} \cdot e^{-k_e t_{\inf}}\right)} \qquad \text{Eq. 3}$$

$$= \frac{120 mg \,/\, 0.5\,Hr}{0.267\,Hr^{-1}} \cdot \frac{1 - e^{-0.267 Hr^{-1} \cdot 0.5 Hr}}{\left(9.7\,mg/L - 1.6\,mg/L \cdot e^{-0.267\,Hr^{-1} \cdot 0.5 Hr}\right)} = 10.7\,L$$

Note that the 10.7 L (0.12 L/Kg) is consistent with dehydration. Using C_o, k_e and V_{ss} estimate a dosing interval, a dose and predict the steady state peak and trough using a practical regimen.

$$\tau = \frac{\ln(7/1)}{0.267\,Hr^{-1}} + 0.5\,Hr = 7.8\,Hr \approx \quad 8\,Hr$$

$$R_0 = 7\ mg/L \cdot 10.7\ L \cdot 0.267\ Hr^{-1}\left[\frac{1-e^{-0.267 Hr^{-1} 8 Hr}}{1-e^{-0.267 Hr^{-1} 0.5 Hr}}\right] = 141.1\ mg/Hr$$

$$Dose = 141.1\ mg/Hr \cdot 0.5\ Hr = 70.55\ mg \approx 70mg$$

Make a practical recommendation and then verify:

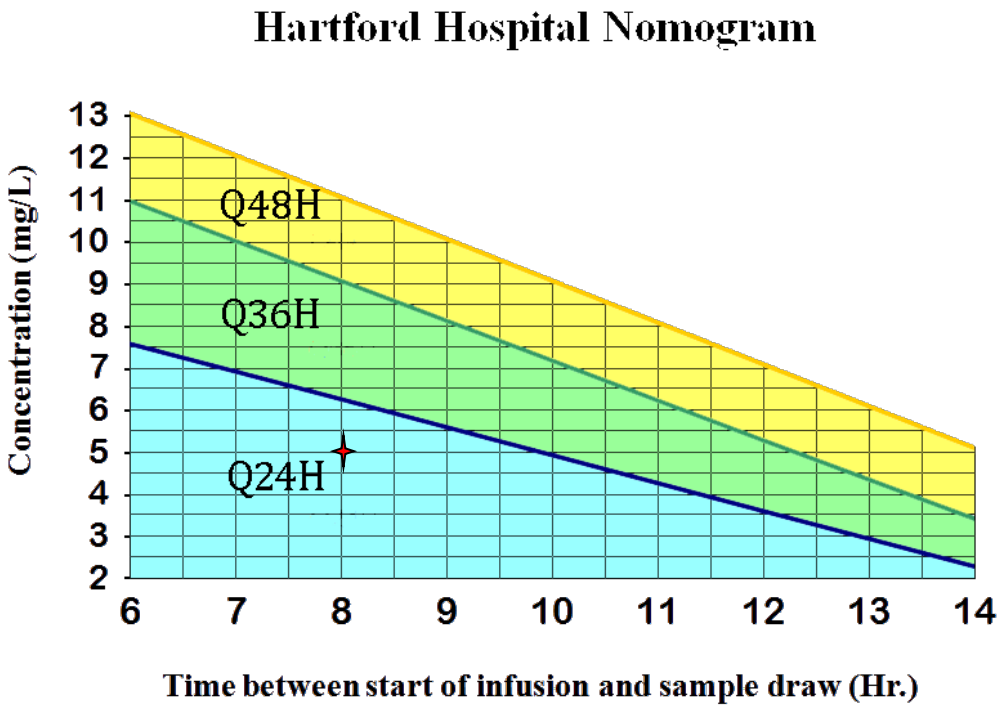
70 mg Gentamicin Q8H for a Pk/Tr = 6.9/0.9 mg/L

$$C_{ss,pk} = \frac{70mg \,/\, 0.5\ Hr.}{10.7\ L \cdot 0.267\ Hr^{-1}} \bullet \frac{\left(1-e^{-0.267 \cdot 0.5}\right)}{\left(1-e^{-0.267 \cdot 8}\right)} = 6.9\ mg/L$$

$$C_{ss,tr} = 6.9\ mg/L \cdot e^{-0.313(8-0.5)} = 0.9\ mg/L$$

Case 4. Following the initial EID regimen of gentamicin, a 66 Kg patient (66 Kg * 7 mg/Kg = 460 mg), a gentamicin level was drawn 8 hours after the infusion was started. The level came back at 5.0 mg/L. What should be the EID regimen of gentamicin for the patient SP based on the Hartford nomogram?

460 mg Gentamicin Q**24**H (Program or nomogram)



Case 5 A 45 YO WM who weighs 89 Kg is 5'11" and has a SrCr = 1.3 mg/dl is going to require vancomycin. Please determine his prospective vancomycin dose.

IBW = 75.3 Kg, DWT = ActBW = 89.0 Kg, and CrCl = 82.0 ml/min
Vss = 62.3 L, Ke = 0.072 Hr^{-1}, $T_{1/2}$ = 9.6 Hr.
1250 mg Vancomycin Q12H for a Pk/Tr = 32.7/15.3 mg/L
Note: 1500 mg Q18H is not a practical Interval

When doing this by hand you would like to do a Tau of 18 Hr., but that is not practical. So try both a Q12H and a Q24H regimen to see which you like better. When you changedose and interval you will see 1000 mg Q12H gives you a Pk/Tr where the PK is a little low. So change interval to Q24H and start adjusting the dose up. At 2000 mg you have a PK in the range, but the TR is too low.

Because of the concentration independent killing the Q12H is better.

Case 6 A 79 YO BF who weighs 84 Kg is 5'1" and has a SrCr = 1.6 mg/dl is going to require an aminoglycoside for an infected surgical wound. Assume she is normally hydrated. Please determine her initial multiple daily dose for **tobramycin**.

IBW = 47.8 Kg, BMI = 35, CrCl Wt & DWT = 62.3 Kg, and CrCl = 28.0 ml/min
Vss = 14.0 L, Ke = 0.097 Hr^{-1}, $T_{1/2}$ = 7.2 Hr.
100 mg Tobramycin Q24H for a Pk/Tr = 7.7/0.8 mg/L

The 20 hour interval recommended is not practical so adjust to Q24H and then try a new dose, 100 mg Q24H would give a P/T = 7.7/0.8 mg/L.

Case 7 A 37 YO WM paraplegic is admitted with a decubitus ulcer and an advancing cellulitis. The patient had one kidney removed when he was a child and has had recurrent urinary tract infections. He now has mild chronic renal impairment. Gram stain indicates the current organism is Gram negative so he will be on placed on amikacin. The patient if 5'9", weighs 90 Kg and has a serum creatinine of 1.4 mg/dl. Patient appears to be normally hydrated. What would be the starting dose?

IBW = 70.7 Kg, DWT = ActWT = 90 Kg, CrClWt = 78.4 Kg
BMI = 29.3 and CrCl = 80.1 ml/min
Vss = 20.3 L, Ke = 0.202 Hr^{-1}, $T_{1/2}$ = 3.4 Hr.
370 mg Amikacin Q6H for a Pk/Tr = 24.7/8.1 mg/L or
425 mg Amikacin Q8H for a Pk/Tr = 24.9/5.5 mg/L

The latter option takes less nursing time, uses less drug per day (425 mgx3 compared to 370mgx4), achieves the same peak blood level and the trough still is reasonable, so the latter would be my recommendation to the physician.

Case 8 A 65 YO WF that you had treated 2 weeks ago with an aminoglycoside now requires vancomycin. Your monitoring form indicates that her actual body weight is 64 Kg and she is 5'10" tall. Her SrCr is stable at 1.0 mg/dl. What starting vancomycin dose does she need?

IBW = 68.5 Kg, DWT = 64 Kg, and CrCl = 56.7 ml/min
Vss = 44.8 L, Ke = 0.051 Hr^{-1}, $T_{1/2}$ = 13.5 Hr.

Noticing that the twice the half-life is 27 hours and a practical interval is just under 2 half-lives, instead of the suggested Q18H go with Q24H, not Q12H (750 mg Q12H would have a trough that is too high –> Pk/Tr = 35.0/20.4 mg/L) Use the change menu to make the changes. An

alternative would be 1250 mg Q24H which would give a P/T of 37.9/11.9, however the following would give a better trough.

1500 mg Vancomycin Q24H for a Pk/Tr = 45.4/14.3 mg/L

Case 9 A 25 year old male is on gentamicin to treat a severe cellulitis at 100 mg Q8H and levels came back at 5.1/1.9 mg/L. The trough was measured at 6:45 am the dose started at 7:00 am and the peak measured at 8:30 am. The chart indicates that he is 5'11" and weights 79 Kg and the patient has experienced a 3 Kg weight gain over the past 2 days. What dosing change would you suggest?

IBW = 75.3 Kg, DWT = ActBW = 79 Kg
Vss = 23.1 L (0.29 L/Kg), Ke = 0.152 Hr^{-1}, $T_{1/2}$ = 4.6 Hr.
140 mg Gentamicin Q12H for a Pk/Tr = 7.0/1.2 mg/L

Make sure you changed T pinf to 1.0 Hr. Recommend this dose, but caution that if the patient returns to normal hydration, i.e. loses the 3 Kg fluid gain, then the resulting levels will be considerably higher, therefore levels should be monitored closely.

Case 10 An 18 YO BM who weighs 69 Kg is 6'1" and has a SrCr = 1.0 mg/dl and has been receiving vancomycin for an infected burn wound. A Pk/Tr were measured around the fourth dose with the Tr at 9:55 pm, the dose started at 10:00 pm and the peak at 1:30 am. The levels were 24.5/8.8 mg/L and the patient had been getting 1250 mg Q12H. What dose would you recommend?

IBW = 79.9 Kg, DWT = ActBW = 69 Kg
Vss = 48.0 L (0.7 L/Kg), Ke = 0.120 Hr^{-1}, $T_{1/2}$ = 5.8 Hr.

Note that the Pk was measured 2 hours after the 1.5 Hr infusion, so in this case C(0) = 31.2 mg/L. A SSpk of 31.2 and a Tr of 8.8 is where we want to be, so **no dosage change** would be recommended. If you wanted to be more aggressive an increase to 1500 mg Q12H would give a Pk/Tr of 36./10.9.

Case 11 A 55 YO BM diabetic is suffering from a wound in his lower right extremity. The wound culture indicated that organism was *Staph. aureus* and the patient has been on 1250 mg vancomycin Q24H for 5 days. The patient is 87 Kg and is 5'8" tall. Levels are measured and came back at 38.3/16.8 mg/L and were measured at 7:15 am, the dose given 8:00 am and then the peak at 11:30 am. What change in dose would you recommend?

IBW = 68.4 Kg, DWT = ActBW = 87 Kg
Vss = 46.9 L (0.54 L/Kg), Ke = 0.042 Hr^{-1}, $T_{1/2}$ = 16.6 Hr.

Note that T early should be changed to 0.75 Hr. and the T pinf must be 2.0 Hr. In this case C(0) = 41.6 mg/L which is too high. If you changed just dose, 1000 mg Q24H it would give a Pk/Tr of 32.7/12.8 mg/L. This is a definite possibility. Making the necessary changes you can see that 1250 mg Q36H would give a Pk/Tr of 33.3/7.9 mg/L where the TR is lower than you would

like. Now you need to know more about the patient. The Q24H regimen is definitely more convenient but if this diabetic patient with poor circulation and poor wound healing also has declining kidney function, you may want go with the more conservative Q36H regimen that has the lower trough.

Case 12 A 42 YO WF weighs 69 Kg is 5'1" and has a SrCr = 0.9 mg/dl and has been receiving gentamicin for a meningitis. A Pk/Tr were measured around the third dose at 7:40 am and 9:15 am and the dose was to be started at 8:00 am. The levels were 5.7/0.4 mg/L on 100 mg Q8H. Her hydration status appears to be normal. What dose would you recommend?

IBW = 47.8 Kg, DWT = AdjWT = 56.3 Kg
Vss = 12.4 L (0.21 L/Kg), Ke = 0.394 Hr^{-1}, $T_{1/2}$ = 1.8 Hr.

Notice that the recommendation appears to target a Pk of 7. We are treating a meningitis, so we want a target near 9. In the retrospective calculation you are not given the option to change your target concentration. However, you can still adjust the dose and interval. If you leave the interval at Q6H you can change the dose to 110 mg to get a Pk/Tr of 8.9/1.0 mg/L. If you want to use the more convenient Q8H interval, and give a dose of 110 mg for a Pk/Tr of 8.4/0.4 mg/L or increase the dose to 120 mg Q8H for a Pk/Tr of 9.2/0.5 mg/L.

120 mg Gentamicin Q8H for a Pk/Tr = 9.2/0.5 mg/L

Case 13 A 70 Y.O. male with a Sr.Cr. of 1.6 mg/dl develops a cellulitis. The Gram stain shows a Gram + cocci. The physician suspects Staph. aureus and wants to start vancomycin. The patient is 5' 9" and weights 92 Kg. The patient was given 1000 mg Q24H and the trough right before the fifth dose was 7.9 mg/dL. What new dose would you recommend?

Here the ratio is 15 mg/dL / 7.9 mg/dL = 1.90 so decrease the interval to Q12H and change the dose.

1000 mg Q12H for a new TR of about 13.4

Case 14 A 61 year old female patient, 5'11" and 102 Kg and with a SrCr = 1.3 mg/dL was given 750 mg Q12H and the trough right before the fifth dose was 18.2 mg/dL. What new dose would you recommend?

Here the ratio is 15 mg/dL / 18.2 mg/dL = 0.82 so just change the dose.

500 mg Q12H for a new TR of about 12.1

Case 15 An Asian female 5'3" and 60 Kg who is 33 Y.O. has been on vancomycin 1000 mg Q12H for 3 days. A single trough level came back at 9.1 mg/dl. What new dose would you recommend?

Here the ratio is 15 mg/dL / 9.1 mg/dL = 1.65 so decrease the interval to Q8H and adjust the dose if necessary, in this case it is not necessary.

1000 mg Q8H for a new TR of about 13.2